

WHAT IS CLAIMED IS:

- 1 1. A method for screening a population of replicable genetic packages
2 to obtain replicable genetic packages that display on their surface a fusion protein that
3 specifically binds to a target molecule, the method comprising:
4 contacting a target molecule with an uncleared cell culture, wherein said
5 culture comprises:
6 (a) replicable genetic packages, each of which displays on its
7 surface a fusion protein that comprises a surface-displayed replicable genetic package
8 polypeptide and a potential binding polypeptide; and
9 (b) cells in which the replicable genetic packages were amplified;
10 wherein said replicable genetic packages that specifically bind to said
11 target molecule form complexes that comprise the target molecule and the replicable
12 genetic packages.
- 1 2. The method of claim 1, wherein said potential binding polypeptide
2 is encoded by a member of a library of nucleic acid molecules.
- 1 3. The method of claim 2, wherein said nucleic acid molecules are
2 cDNA molecules.
- 1 4. The method of claim 2, wherein said nucleic acid molecules are
2 recombinant products.
- 1 5. The method of claim 1, wherein said method further comprises
2 separating from said complexes cells and/or replicable genetic packages that do not
3 specifically bind to said target molecule.
- 1 6. The method of claim 5, wherein at least 70% of the cells originally
2 present in the culture are removed.
- 1 7. The method of claim 6, wherein at least 90% of the cells originally
2 present in the culture are removed.
- 1 8. The method of claim 5, wherein said cells and unbound replicable
2 genetic packages are separated from said complexes using aspiration.

1 9. The method of claim 5, wherein the method further comprises
2 eluting said replicable genetic packages that specifically bind to said complexes.

1 10. The method of claim 1, wherein the presence of said complexes
2 that comprise the target molecule and the replicable genetic packages is assessed by
3 contacting the complexes with a detection reagent that binds to said replicable genetic
4 packages.

1 11. The method of claim 10, wherein said detection reagent comprises
2 an antibody.

1 12. The method of claim 10, wherein the complexes are contacted with
2 the detection reagent in the presence of the cells.

1 13. The method of claim 1, wherein the replicable genetic packages are
2 selected from the group consisting of bacteriophage and eukaryotic viruses.

1 14. The method of claim 1, wherein said target molecule is
2 immobilized on a solid support.

1 15. The method of claim 14, wherein said solid support is selected
2 from the group consisting of: a bead, a chip, a microtiter plate, a prokaryotic cell and a
3 eukaryotic cell.

1 16. The method of claim 1, wherein said target molecule is selected
2 from the group consisting of: a polypeptide, a nucleic acid, an RNA, a DNA, a small
3 organic molecule, and a carbohydrate.

1 17. The method of claim 1, wherein said potential binding polypeptide
2 is an antibody.

1 18. The method of claim 17, wherein said antibody is a scFv or a Fab.

1 19. The method of claim 1, wherein said method is performed on an
2 automated laboratory workstation.

1 20. A composition comprising:

- 2 (a) population of replicable genetic packages, each of which
3 displays on its surface a fusion protein that comprises a surface-displayed replicable
4 genetic package polypeptide and a potential binding polypeptide; and
5 (b) a complex that comprises a target molecule and one or more
6 members of the population of replicable genetic packages that specifically bind to said
7 target molecule; and
8 (c) cells in which the replicable genetic packages were amplified.

1 21. The composition of claim 20, wherein said replicable genetic
2 packages are selected from the group consisting of bacteriophage and eukaryotic viruses.

1 22. The composition of claim 20, wherein said target molecule is
2 immobilized on a solid support.

1 23. The composition of claim 20, wherein said solid support is selected
2 from the group consisting of: a bead, a chip, a microtiter plate, a prokaryotic cell and a
3 eukaryotic cell.

1 24. The composition of claim 20, wherein said target molecule is
2 selected from the group consisting of: a polypeptide, a nucleic acid, an RNA, a DNA, a
3 small organic molecule, and a carbohydrate.

1 25. The composition of claim 20, wherein said potential binding
2 polypeptide is an antibody.

1 26. The composition of claim 25, wherein said antibody is a scFv or a
2 Fab.

1 27. The composition of claim 20, wherein the composition further
2 comprises a detection reagent that specifically binds to the replicable genetic packages.